## Science

This phylogenetic tree depicts the relationships between members of this complete superfemily of human protein kinases. Protein kinases constitute one of the largest human gene families and are key regulators of cell function. The \$18 human protein kinases control protein activity by catalyzing the addition of a negatively charged phosphate group to other proteins. Protein kinases mediate a wide variety of bloogical processes, especially those that carry signals from the self membrane to infracellular targets and coordinate complex biological functions.

Most protein kinases belong to a single superfamily of enzymes whose catalytic domains are related in sequence and structure. The main diagram flustrates the similarity between the protein esquences of those catalytic domains. Each kinase is at the tip of a branch, and the similarity between various kinases is inversely related to the distance between their positions on the tree diagram. Most kinases fall into small families of highly related sequences, and most

families are part of larger groups. The seven major groups are labeled and colored distriction of the tree, colored gray. The relationships shown tree can be used to predict protein substrates and biological function for many of the our uncharacterized kinases presented here.

The Inset diagram shows trees for seven atypical protein kinase tamilies. These in nave verified or strongly predicted kinase activity, but have little or no sequence similar members of the protein kinase superfamily. A further eight stypical protein kinases in stamilies of one or two genes are not shown.

